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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/741,960 12/20/00 METSPALU

A 18056/00301

EXAMINER

HM12/0330

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ART UNIT

PAPER NUMBER

1655

DATE MAILED:

09/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/741,960

Applicant(s)

METSPALU ET AL.

Examiner

Bradley L. Sisson

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____.

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1650, Art Unit 1655, and has been assigned to Primary Examiner Bradley L. Sisson.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Estonia on 21 April 1999. It is noted, however, that applicant has not filed a certified copy of the Estonian application as required by 35 U.S.C. 119(b).

Claim Objections

3. Claims 2-12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 2-12 (as well as claims 13-15) all depend from claim 12.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-15, drawn to a fluorescence detector, are not adequately described so as to reasonably suggest that applicant was in possession of same at the time of filing. It is noted with particularity that the specification neither incorporates by reference prior art devices and subsequently teaches how the claimed device is modified; nor provides detailed description as to how the claimed device is to be manufactured, assembled and ultimately utilized. In support of this position, attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*". The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

For the above reasons, and in the absence of convincing evidence to the contrary, the device of claims 1-15 is not adequately described by the specification so as to satisfy the requirements of 35 USC 112, first paragraph.

5. Claims 16 and 17 are not adequately described by the instant specification so as to reasonably suggest that applicant was in possession of a functional method of "detecting and analyzing a specific nucleic acid sequence" (claim 16) or in possession of a method for "analyzing the sequence of a polynucleotide of interest." At best the specification provides a

most basic of general guidance as to what the claimed methods are to be capable of producing. Such generalities, however, do not rise to the level of an adequate written description of either method.

6. For the above reasons, and in the absence of convincing evidence to the contrary, the

7. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided

The amount of guidance provided, be it in regard to the claimed device (claims 1-15) or the two methods (claims 16 and 17), the guidance is most limiting.

The Presence or Absence of Working Examples

There are no working examples be it for the manufacture or use of the device; or for practicing the two methods.

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the art has advanced to the point that there are numerous art-recognized problems confronting the performance of nucleic acid assays, including hybridization-based assays, as claimed instantly and for which the device is to be utilized in. As set forth in Carrico, (US Patent 5,200,313) the extent and specificity of hybridization is affected by the following principal conditions:

1. The purity of the nucleic acid preparation.
2. Base compositions of the probe - G-C base pairs will exhibit greater thermal stability than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.

3. Length of homologous base sequences- Any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.

4. Ionic strength- The rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.

5. Incubation temperature- Optimal reannealing occurs at a temperature about 25 - 30 °C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.

6. Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.

7. Denaturing reagents- The presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.

8. Incubation- The longer the incubation time, the more complete will be the hybridization.

9. Volume exclusion agents- The presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic

strength, and increasing temperature, e.g., 0.1X SSC for 30 minutes at 65 °C, will, with increasing effectiveness, remove non-fully complementary hybridization products.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have sufficient breadth of scope so to encompass genera of devices as well as genera of methods of analyzing nucleic acid sequences. With regard to the devices, it is noted that there need not be structural relatedness between the various components of the device. Clearly, the specification has not enabled the manufacture, and much less the use, of such a device. Further, applicant has seemingly left it up to the public in determining just how the various methods are to be practiced as neither the starting materials nor any reaction conditions have been provided.

The absence of such essential components undoubtedly calls for the expenditure of undue experimentation on the part of the public. The situation at hand is analogous to that in

Genentech v. Novo Nordisk A/S 42 USPQ2d 1001. As set forth in the decision of the Court:

“ ‘[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.’ *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) (‘[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.’).

"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

"It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

For the above reasons, and the absence of convincing evidence to the contrary, the inventions of claims 1-17 have not been found to be enabled by the specification as originally filed.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: That which exists between elements a), b) and c).

11. Claims 1, 5, 6, 8-13 recites the limitation "said waveguide support". There is insufficient antecedent basis for this limitation in the claim.

12. Claims 2-6 recites the limitation "the light source". There is insufficient antecedent basis for this limitation in the claims.

13. Claim 5 is confusing as to how the revolution of a hexahedron about an axis that is perpendicular, yet not necessarily intersecting with, a light beam, has the capacity of "placing said light source into said waveguide support."

14. Claim 7 recites the limitation "the waveguide" in line 2. There is insufficient antecedent basis for this limitation in the claim.

15. Claim 7 is indefinite with respect to what constitutes "a shaped smallled [sic] than an edge of said waveguide."

16. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: That which exists between the mirror and any other element of the "fluorescence detector."

17. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a

gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: That which exists between the "optical prism" and the other elements of the device.

18. Claim 11 recites the limitation "said optical prism" in line 2. There is insufficient antecedent basis for this limitation in the claim.

19. Claim 11 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: That which exists between the waveguide support, the optical prism, transparent fluid, and any other elements of the device.

20. Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: that which exists between the waveguide support and the other elements of the device.

21. Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: That which must exist between the "bandpass filters" (claim 14) and the "personal computer" (claim 15) with the other elements of the device.

22. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

§ 2172.01. The omitted steps are: those that will result in the actual "detection and analysis [of] a specific nucleic acid sequence." As presently worded, there are a plurality of oligonucleotides affixed to the surface of a waveguide support. There is no requirement that the oligonucleotides be placed at any given location, e.g., an addressable array, nor is there any requirement that one have prior knowledge of which oligonucleotide possesses a fluorescent nucleotide. Accordingly, the detection of a fluorescent signal would not in and of itself result in any analysis of any oligonucleotide. While one is to employ a computer, the presence of a fluorescent signal, without more, does not impart an analysis of a nucleic acid. There must exist some correlation between the signal and the nucleic acid. The claimed method does not allow for such a correlation.

23. As presently worded, the claimed method has sufficient breadth of scope so to encompass performing any number of reactions simultaneously, including multiplex PCR, nucleic acid purification, mutation detection, sequencing, and the like. The claim does not set forth how unused reactants are removed, and if not removed, how any fluorescent signal, a.k.a., "results" are to be adjusted for such effects.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

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organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
March 28, 2001